

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment encoding an isoleucyl-tRNA synthase comprising a member selected from the group consisting of:

5 (a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in SEQ ID NO:2, 4, 6 and 8;

(b) an isolated nucleic acid fragment that is complementary to (a).

10 2. The isolated nucleic acid fragment of Claim 1 wherein nucleic acid fragment is a functional RNA.

3. The isolated nucleic acid fragment of Claim 1 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:1, 3, 5 and 7.

15 4. A chimeric gene comprising the nucleic acid fragment of Claim 1 operably linked to suitable regulatory sequences.

5. A transformed host cell comprising the chimeric gene of Claim 4.

6. An isoleucyl-tRNA synthase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4, 6 and 8.

20 7. An isolated nucleic acid fragment encoding a lysyl-tRNA synthetase comprising a member selected from the group consisting of:

(a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:10, 12, 14, and 16;

25 (b) an isolated nucleic acid fragment that is complementary to (a).

8. The isolated nucleic acid fragment of Claim 7 wherein nucleic acid fragment is a functional RNA.

30 9. The isolated nucleic acid fragment of Claim 7 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:9, 11, 13 and 15.

10. A chimeric gene comprising the nucleic acid fragment of Claim 7 operably linked to suitable regulatory sequences.

11. A transformed host cell comprising the chimeric gene of Claim 10.

35 12. A lysyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:10, 12, 14 and 16.

13. An isolated nucleic acid fragment encoding a phenylalanyl-tRNA synthetase comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:18, 20, 22 and 24;
- (b) an isolated nucleic acid fragment that is complementary to (a).

14. The isolated nucleic acid fragment of Claim 13 wherein nucleic acid fragment is a functional RNA.

15. The isolated nucleic acid fragment of Claim 13 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:17, 19, 21 and 23.

16. A chimeric gene comprising the nucleic acid fragment of Claim 13 operably linked to suitable regulatory sequences.

17. A transformed host cell comprising the chimeric gene of Claim 16.

18. A phenylalanyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:18, 20, 22 and 24.

19. An isolated nucleic acid fragment encoding a prolyl-tRNA synthetase comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding an amino acid sequence of at least 152 contiguous amino acids and that is at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:26, 28 and 30;
- (b) an isolated nucleic acid fragment that is complementary to (a).

20. The isolated nucleic acid fragment of Claim 19 wherein nucleic acid fragment is a functional RNA.

21. The isolated nucleic acid fragment of Claim 19 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:25, 27 and 29.

22. A chimeric gene comprising the nucleic acid fragment of Claim 19 operably linked to suitable regulatory sequences.

23. A transformed host cell comprising the chimeric gene of Claim 22.

24. A prolyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:26, 28 and 30.

25. A method of altering the level of expression of an aminoacyl-tRNA synthetase in a host cell comprising:

- (a) transforming a host cell with the chimeric gene of any of Claims 4, 10, 16 and 22; and
- (b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene

5 wherein expression of the chimeric gene results in production of altered levels of an aminoacyl-tRNA synthetase in the transformed host cell.

26. A method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence encoding an aminoacyl-tRNA synthetase comprising:

- 10 (a) probing a cDNA or genomic library with the nucleic acid fragment of any of Claims 1, 7, 13 and 19;
- (b) identifying a DNA clone that hybridizes with the nucleic acid fragment of any of Claims 1, 7, 13 and 19;
- (c) isolating the DNA clone identified in step (b); and
- (d) sequencing the cDNA or genomic fragment that comprises the clone

15 wherein the sequenced nucleic acid fragment encodes all or a substantial portion of the amino acid sequence encoding an aminoacyl-tRNA synthetase.

27. A method of obtaining a nucleic acid fragment encoding a substantial portion of an amino acid sequence encoding an aminoacyl-tRNA synthetase comprising:

- 20 (a) synthesizing an oligonucleotide primer corresponding to a portion of the sequence set forth in any of SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27 and 29; and
- (b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a) and a primer representing sequences

25 wherein the amplified nucleic acid fragment encodes a substantial portion of an amino acid sequence encoding an aminoacyl-tRNA synthetase.

28. The product of the method of Claim 26.

29. The product of the method of Claim 27.

30 30. A method for evaluating at least one compound for its ability to inhibit the activity of an aminoacyl-tRNA synthetase, the method comprising the steps of:

- (a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding an aminoacyl-tRNA synthetase, operably linked to suitable regulatory sequences;
- 35 (b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of the aminoacyl-tRNA synthetase encoded

by the operably linked nucleic acid fragment in the transformed host cell;

- (c) optionally purifying the aminoacyl-tRNA synthetase expressed by the transformed host cell;
- (d) treating the aminoacyl-tRNA synthetase with a compound to be tested; and
- (e) comparing the activity of the aminoacyl-tRNA synthetase that has been treated with a test compound to the activity of an untreated aminoacyl-tRNA synthetase,

thereby selecting compounds with potential for inhibitory activity.